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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/564,070	03/03/2006	Sutisak Kitareewan	DC0266/US.NP	5026
26259 7590 02/28/2011 LICATA & TYRRELL P.C. 66 E. MAIN STREET MARLTON, NJ 08053				
EXAMINER MARTIN, PAUL C				
ART UNIT 1657		PAPER NUMBER		
NOTIFICATION DATE 02/28/2011		DELIVERY MODE ELECTRONIC		

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

porcilly@licataandtyrrell.com

Office Action Summary

Application No.

10/564,070

Applicant(s)

KITAREEWAN ET AL.

Examiner

PAUL C. MARTIN

Art Unit

1657

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 01 February 2011.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) g is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) g is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date _____
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date _____
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: _____

DETAILED ACTION

Claim 8 is pending in this application and was examined on its merits.

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 02/11/2011 has been entered.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claim 8 remains rejected under 35 U.S.C. § 103(a) as being unpatentable over Yoshida *et al.* (1996) in view of Bard *et al.* (1977) for reasons of record set forth in the prior actions.

Response to Arguments

Applicant's arguments (Remarks, Pgs. 4-8) with respect to claim 8 have been considered but are moot in view of the new ground(s) of rejection below.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. § 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claim 8 is newly rejected under 35 U.S.C. § 103(a) as being unpatentable over Bard *et al.* (1977) in view of Yoshida *et al.* (1996).

Bard *et al.* teaches that at higher than physiological concentrations retinoids destabilize membranes causing the release of lysosomal enzymes and that the effect can be followed by metachromatic staining and by measuring the appearance of proteoglycan fragments in the medium of organ cultures of rabbit ear cartilage (Pg. 115, Column 1, Lines 25-36 and Column 2, Lines 1-3

Bard *et al.* does not teach a method comprising contacting a cell expressing PML/RAR α and detecting whether said agent destabilizes lysosomes of the cell as determined by vital staining of lysosomes or release of lysosomal proteins into the cytosol; and increases lysosomal-dependent PML-RAR α protein degradation.

Yoshida *et al.* teaches a method comprising contacting an APL (acute promyelocytic leukemia) cell that expresses PML/RAR α with the anti-cancer agent ATRA (*all-trans-retinoic acid*) (Pg. 2946, Column 2, Lines 22-29).

It would have been obvious to one of ordinary skill in the art at the time of the instant invention to modify the teachings of Bard *et al.* whom teaches that retinoid compounds destabilize membranes causing the release of lysosomal enzymes and that the effect can be followed by metachromatic staining and by measuring the appearance of proteoglycan fragments in the medium of organ cultures of rabbit ear cartilage to use cells expressing PML-RAR α because the method of Bard *et al.* is not limited to any particular cell type and thus it would have been obvious to one of ordinary skill in the art that any cell type could be exposed to retinoids and monitored for lysosomal destabilization. Those of ordinary skill in the art would have also been aware that as lysosomes destabilize, they release lysosomal enzymes into the cytosol which would actively degrade any proteins they encounter, including the protein PML-RAR α , if present.

Therefore, the combined method of Bard *et al.* and Yoshida *et al.* would serve to identify an agent (retinoic acid) causing the destabilization of lysosomes in cells expressing PML-RAR α and inherently increasing lysosomal-dependent PML-RAR α protein degradation (in addition to many other proteins). The limitation that the protein degradation be "lysosomal dependent" is inherently met as the destabilization of the lysosomes releases enzymes and would not otherwise occur, making the resulting protein degradation necessarily "lysosomal dependent".

No Claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to PAUL C. MARTIN whose telephone number is (571)272-3348. The examiner can normally be reached on M-F 12pm-8pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jon Weber can be reached on 571-272-0925. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Paul Martin
Examiner
Art Unit 1657

02/23/2011

/Rebecca E. Prouty/
Primary Examiner,
Art Unit 1652